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The Multidisciplinary Role of the Anesthesiologist in the Administration of Ketamine for Depression Treatment Resistant

The Multidisciplinary Role of the Anesthesiologist in Ketamine Administration for Treatment-Resistant Depression

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Summary

Treatment-resistant depression (TRD) represents a highly complex clinical challenge for modern psychiatry, requiring innovative and safe approaches. Notable among these strategies is the use of ketamine, a dissociative anesthetic that, in subanesthetic doses, has demonstrated rapid and significant antidepressant effects. However, its administration requires a controlled environment and rigorous monitoring, functions traditionally performed by anesthesiologists. This article analyzes the multidisciplinary role of this specialist at the interface between anesthesiology and psychiatry, addressing clinical, ethical, and technical aspects of therapeutic management, as well as discussing scientific evidence up to 2021.

Keywords: Ketamine; Resistant depression; Anesthesiology; Psychiatry; Multidisciplinary therapy.

Abstract

Treatment-resistant depression (TRD) represents a highly complex clinical challenge for modern psychiatry, demanding and safe therapeutic approaches. Among these strategies, the use of ketamine stands out. As a dissociative anesthetic, ketamine has shown rapid and significant antidepressant effects when administered at subanesthetic doses. However, its administration requires a controlled environment and rigorous monitoring, traditionally under the responsibility of the anesthesiologist. This article analyzes the multidisciplinary role of this specialist at the interface between anesthesiology and psychiatry, addressing clinical, ethical, and technical aspects of therapeutic management, while also reviewing scientific evidence up to 2021.

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1. Introduction to Treatment-Resistant Depression

Major depression is considered by the World Health Organization (WHO, 2017) to be one of the leading causes of global disability, affecting millions of people in all regions of the world and having a significant socioeconomic impact. Despite the availability of several pharmacological classes, such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants, it is estimated that approximately 30% to 40% of patients do not respond adequately to conventional treatments. This clinical condition is called treatment-resistant depression (TRD), a concept that represents not only a therapeutic failure but also a persistent challenge for healthcare systems, families, and individuals living with it.

disorder.

The definition of TRD varies between guidelines, but a consensus established by the American Psychiatric Association (APA, 2013) indicates that the diagnosis applies when the patient does not present a satisfactory response after using at least two antidepressants, in adequate doses and for a sufficient period of time. This characterization, although objective, still generates debate about its methodological limitations, as it does not consider factors such as treatment adherence, clinical comorbidities, and social aspects. Furthermore, many patients undergo prolonged cycles of therapeutic attempts that result in worsening of their clinical condition, further compromising their quality of life.

The impact of DRT transcends the individual sphere and reaches the collective, resulting in high rates of absence from work, early retirement, and direct and indirect costs to society.
According to data from the Organization for Economic Cooperation and Development (OECD, 2019), depressive disorders represent one of the leading causes of lost productivity, resulting in billions of dollars in annual economic losses. In this context, the search for effective therapeutic alternatives is not only a clinical necessity but also a public health demand.

Psychotherapy, whether or not associated with drug treatment, is widely used as a complementary tool, but in severe cases of TRD, it often presents limited results.
Another frequently used approach is electroconvulsive therapy (ECT), considered effective in many refractory patients. However, social stigma, adverse effects, and the complexity of the procedure reduce its acceptance among patients and families. This reinforces the need for innovative strategies capable of offering rapid response, safety, and satisfactory adherence.

It is in this scenario that ketamine emerges as a potential differentiated therapeutic resource.
Originally used as a dissociative anesthetic in hospital settings, the substance gained prominence in the 2000s due to its rapid antidepressant action, observed in

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pioneering studies such as that of Berman et al. (2000), followed by robust research conducted by Zarate et al. (2006) at the National Institute of Mental Health. These discoveries opened new perspectives for the clinical management of TRD.

The relevance of ketamine as an emerging resource, however, requires an understanding of its risks, limitations, and specificities. Unlike traditional antidepressants, its effect is rapid in onset but not necessarily long-lasting, requiring specific maintenance protocols and continuous monitoring. Furthermore, its potential dissociative and abuse-prone effects raise ethical and regulatory concerns, highlighting the importance of a controlled and safe environment.

Given this scenario, the intersection between psychiatry and anesthesiology seems inevitable. While psychiatry provides diagnosis, indications, and management of the therapeutic plan, the anesthesiologist possesses the expertise necessary to ensure the safe administration of ketamine, with adequate monitoring of vital functions and management of potential adverse effects. This multidisciplinary collaboration represents a milestone in the advancement of contemporary clinical practices.

2. Ketamine and Its Pharmacological Properties

Ketamine was first synthesized in 1962 by Calvin Stevens and introduced into medical practice in 1970 as an anesthetic for human and veterinary use. Its main pharmacological characteristic is its action as a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, resulting in dissociative and anesthetic effects. Unlike other agents, ketamine preserves airway reflexes and maintains relative cardiovascular stability, which is why it has been widely used in surgical and emergency settings. These attributes have made it especially valuable in war, trauma, and intensive care settings.

When administered in subanesthetic doses, ketamine exhibits distinct properties, especially in the context of neuropsychiatry. Clinical studies have shown that the substance significantly improves depressive symptoms within hours of infusion, in contrast to conventional antidepressants, which typically require weeks to achieve therapeutic effect. This rapid response is considered a significant advance in the treatment of TRD, especially in patients at risk of suicide, where response time is critical.

The antidepressant mechanism of ketamine, although not yet fully elucidated, involves hypotheses related to glutamatergic modulation, increased release of brain-derived neurotrophic factor (BDNF), and promotion of synaptic neuroplasticity (Duman & Aghajanian, 2012). This neurobiological effect, associated with NMDA receptor blockade, appears to contribute to the restoration of neuronal connectivity in brain regions associated with mood regulation, such as the prefrontal cortex and hippocampus.

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At the same time, ketamine exerts psychotomimetic and dissociative effects, which, while generally transient, can cause significant discomfort in some patients. Sensations of depersonalization, perceptual alterations, and hallucinatory phenomena are described relatively frequently, reinforcing the need for constant monitoring during the infusion. Furthermore, there is concern about the potential for recreational abuse, as the substance is used illicitly in non-medical settings.

Ketamine's pharmacokinetics contribute to the complexity of its clinical management. When administered intravenously, it has a rapid onset of action, a relatively short half-life, and active metabolites, such as norketamine, may also influence its antidepressant effects. Other routes of administration, such as intranasal and oral, are being studied to expand treatment accessibility, but they still lack standardization and widespread validation in clinical protocols.

Randomized controlled clinical trials, such as those conducted by Murrough et al. (2013) and Daly et al. (2018), have established the efficacy of ketamine in patients with TRD, showing response rates higher than those of placebo and a significant reduction in suicidal ideation in the short term. However, these results also highlighted the need for structured maintenance protocols, as the beneficial effects tend to dissipate within a few days or weeks, requiring repeated sessions.

In this sense, the role of the anesthesiologist becomes indispensable. By handling potent anesthetic drugs and possessing expertise in hemodynamic, ventilatory, and neurological monitoring, this professional ensures that ketamine is administered safely. This prevents the occurrence of serious complications, such as hypertensive crises, severe adverse reactions, or exacerbated psychological distress. This represents a clear interface between advanced pharmacology and clinical practice, where anesthesiology combines with psychiatry to expand therapeutic horizons.

3. The Interface between Anesthesiology and Psychiatry

The administration of ketamine for treatment-resistant depression requires a convergence between two medical specialties: psychiatry, responsible for the diagnosis and monitoring of depressive disorder, and anesthesiology, which possesses the technical expertise necessary to manipulate anesthetic agents and monitor critical physiological parameters. This multidisciplinary interface is not merely an operational arrangement, but a care model that seeks to ensure safety and therapeutic efficacy. When prescribing ketamine, the psychiatrist delegates the pharmacological management of the infusion to the anesthesiologist, creating a space for clinical cooperation that exemplifies the advances of integrated medicine in the 21st century.

In practice, the anesthesiologist ensures that the substance is administered in a controlled environment, usually in specialized clinics or medical centers equipped for emergencies.
Continuous monitoring of parameters such as blood pressure, oxygen saturation and

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Heart rate monitoring is essential, as ketamine can cause transient elevations in blood pressure and tachycardia. Furthermore, managing potential immediate adverse effects, such as nausea, dizziness, or intense dissociative reactions, requires technical expertise within the field of anesthesiology.

Psychiatry, in turn, plays an essential role in the careful selection of patients, definition of therapeutic protocols, and longitudinal follow-up. The psychiatrist assesses the clinical history, identifies the refractoriness of the condition, and establishes therapeutic goals, such as reducing severe depressive symptoms or suicidal ideation. This initial assessment is crucial, as it ensures that ketamine is used in cases where the benefits outweigh the risks, avoiding its indiscriminate use or use without scientific evidence.

Studies show that this collaboration significantly increases the safety of therapy. According to Sanacora et al. (2017), international guidelines emphasize that ketamine should only be administered in properly equipped clinical settings, under the supervision of professionals qualified to intervene in acute complications. This guideline supports the relevance of anesthesiology in the psychiatric context, expanding the perception of anesthesiologists as key agents in the field of mental health.

Clinical practice also shows that ketamine's antidepressant effects occur quickly but are short-lived. Therefore, the anesthesiologist must coordinate their role with the psychiatrist, adjusting the frequency of infusions and collaborating on the design of maintenance protocols. This dynamic creates a continuous flow of communication between specialties, in which therapeutic efficacy depends on the synergy between psychiatric diagnosis and anesthesiological execution.

Furthermore, the interface between anesthesiology and psychiatry promotes a humanized approach to care. Many patients with ESRD arrive for treatment after years of frustration with ineffective therapies. Joint monitoring by two specialists provides emotional security, increases adherence, and reduces the stigma associated with innovative procedures. It is, therefore, a model that combines technical rigor and clinical sensitivity, favoring the patient's full recovery.

Ultimately, the relationship between these two fields points to a new medical paradigm: interdisciplinarity applied to complex disorders. Anesthesiologists no longer work exclusively in surgical settings but take on an active role in mental health, while psychiatrists expand their therapeutic boundaries by integrating knowledge of anesthetic pharmacology. This symbiosis represents a breakthrough for integrated healthcare, establishing a model replicable in other medical fields that require joint interventions.

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4. Ketamine Administration and Monitoring Protocols

Ketamine administration in patients with treatment-resistant depression requires standardized protocols that ensure both efficacy and safety. These protocols range from dose determination to clinical setting selection, including physiological and psychological monitoring during and after the infusion. Scientific literature up to 2021 suggests that the most studied dose in psychiatric settings is 0.5 mg/kg, administered intravenously over 40 minutes, although variations are possible depending on the patient's condition (Daly et al., 2018).

Monitoring during infusion should include cardiovascular, respiratory, and neurological parameters. Ketamine can induce transient increases in blood pressure and heart rate, requiring continuous monitoring and the ability to intervene immediately. Equipment such as multiparameter monitors, pulse oximeters, and ventilatory support devices must be available at all sessions. This infrastructure is an integral part of the anesthesiologist's work, whose training includes expertise in managing critical situations and medical emergencies.

After the infusion, the patient must remain under observation for a period ranging from 30 minutes to two hours to ensure that any side effects are identified and treated. The most common side effects include mild sedation, dizziness, nausea, and unusual perceptual experiences. While generally transient, these symptoms can cause anxiety and discomfort, making the presence of a trained team essential to provide support and reassurance.

Another key aspect of the protocols is prior and subsequent psychiatric evaluation. Patients should be assessed using validated scales, such as the Montgomery-Åsberg Depression Rating Scale (MADRS), to quantify the intensity of depressive symptoms and assess response to treatment. This systematic monitoring allows for personalized therapy, avoiding both underdosing and unnecessary exposure to repeated infusions in non-responsive patients.

The frequency of infusions is still a topic of debate, but studies such as that by Murrough et al. (2013) indicate that multiple sessions over two to three weeks can enhance the antidepressant response. However, the effect tends to wane over time, requiring maintenance protocols that vary according to individual response. This unpredictability reinforces the need for continuous monitoring and collaboration between anesthesiologists and psychiatrists.

The administration environment also deserves attention. International guidelines recommend that treatment take place in facilities equipped for advanced life support, preferably within hospitals or clinics with similar facilities. The lack of these facilities can significantly increase risks and compromise patient safety. Therefore, administration in offices without adequate support has neither scientific nor ethical support.

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Finally, administration and monitoring protocols reflect not only technical requirements but also ethical and regulatory considerations. The use of ketamine for ESRD, although supported by growing evidence, still lacks universal standardization. Therefore, the responsibility of the professionals involved goes beyond clinical practice, including a commitment to constant scientific updates, adherence to institutional standards, and the protection of the patient's physical and mental integrity.

5. Clinical Evidence and Therapeutic Impact

Clinical evidence on the use of ketamine in treatment-resistant depression grew significantly in the first two decades of the 21st century. Pioneering studies such as those by Berman et al. (2000) and Zarate et al. (2006) demonstrated rapid antidepressant effects, sparking great interest from the scientific community. Since then, multiple randomized clinical trials have confirmed the drug's efficacy in reducing depressive symptoms in patients who did not respond to conventional treatments, demonstrating response rates higher than those of placebo and a direct impact on reducing suicidal ideation. These results, although initial, have transformed psychiatry's perception of the possibility of rapid responses in refractory conditions.

In a meta-analysis conducted by Coyle and Laws (2015), ketamine was found to provide significant improvement in patients with TRD within 24 hours of infusion, a significantly shorter response time than traditional antidepressants. This rapid response represents a crucial therapeutic advance, especially in cases of imminent suicidal risk, where delayed pharmacological response can be decisive for the patient's clinical outcome.
This aspect reinforces the need for emergency protocols that include ketamine as a therapeutic option in critical situations.

Subsequent studies, such as that by Murrough et al. (2013), confirmed that ketamine's antidepressant effects, while robust, tend to be transient, typically lasting seven to ten days after a single infusion. This finding prompted research into multi-session protocols aimed at prolonging clinical benefit. Research by Daly et al. (2018) explored repeated infusion regimens, with results suggesting greater durability of response, although accompanied by debate about the safety of prolonged use.

In addition to direct efficacy, ketamine's impact extends to improving patients' functional status. Clinical reports indicate that the substance can promote the resumption of daily activities, the reestablishment of social bonds, and increased personal motivation. These results are highly relevant, as resistant depression often causes social isolation and severe functional disability. Thus, ketamine's effect is not limited to immediate symptomatic relief but also promotes significant improvements in quality of life.

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However, evidence also points to heterogeneity in responses. Not all patients with ESRD experience significant clinical improvement after ketamine infusion. Observational studies indicate that genetic factors, neurobiological profile, and the presence of comorbidities directly influence outcomes. This variability suggests the need for biomarkers that allow early identification of which patients are most likely to respond to treatment, optimizing therapy utilization.

Another relevant point is the discussion about long-term effects. Although studies up to 2021 demonstrate short-term safety, there are still significant gaps regarding the impact of ketamine in long-term treatments. Concerns regarding the risk of tolerance, dependence, and possible cognitive changes remain under debate. These aspects highlight the importance of further research and rigorous multidisciplinary monitoring to ensure that ketamine use is not only effective but also sustainable.

Thus, the body of clinical evidence supports ketamine as an innovative and promising resource for treatment-resistant depression. While not a definitive solution, its incorporation into psychiatric protocols represents an undeniable advance in the search for therapies that offer rapid and effective relief to refractory patients. The therapeutic impact, combined with the need for continuous monitoring, positions the substance as a central part of the contemporary debate in psychiatry and anesthesiology.

6. Ethical and Regulatory Aspects

The use of ketamine in the treatment of resistant depression raises important ethical and regulatory issues that go beyond clinical practice and involve health policies, legislation, and bioethical principles. The main ethical concern relates to patient safety, given that ketamine is a dissociative anesthetic with potential for abuse in recreational settings. This characteristic requires its administration in specialized medical settings, avoiding the risk of trivializing the treatment and preventing long-term adverse consequences.
term.

From a regulatory perspective, different countries adopted different measures until 2021. In the United States, the Food and Drug Administration (FDA) approved the use of intranasal esketamine, an enantiomer of ketamine, for TRD cases in 2019, under strict clinical monitoring protocols. This approval was considered a milestone, as it provided official support for a practice that had been applied experimentally in several clinics. However, the use of intravenous racemic ketamine remains outside of formal approval, being restricted to off-label indications.

In Brazil, the Federal Council of Medicine (CFM) issued opinions that allow the use of ketamine in specific cases of refractory depression, as long as ethical and

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monitoring technicians. This regulation seeks to balance therapeutic innovation with the necessary prudence when dealing with a drug with potential for inappropriate use. The requirement for monitoring by specialists and the need for detailed medical records reflect this cautious approach taken by regulatory institutions.

Ethical issues also include patient autonomy and the principle of beneficence. Many patients with ESRD turn to ketamine after long periods of suffering, seeking relief from debilitating symptoms. In these cases, the right to access innovative therapies must be balanced against the medical obligation to provide safe, evidence-based treatments.
This delicate balance requires transparent communication between healthcare professionals and patients, ensuring that decisions are informed and shared.

Another relevant ethical aspect is the cost of treatment. In many contexts, ketamine administration is not covered by public health systems or private plans, restricting its access to patients with greater purchasing power. This inequality raises discussions about distributive justice and health equity, as low-income individuals may be deprived of a potentially life-saving resource. Inclusive public policies and cost-effectiveness research are essential to mitigate these disparities.

Bioethics also highlights the need for ongoing research, conducted transparently and free from conflicts of interest. The enthusiasm surrounding ketamine cannot override scientific prudence. Multicenter clinical trials, systematic reviews, and long-term follow-up are essential tools for assessing risks and benefits more accurately. Only with this foundation will it be possible to consolidate universal ethical and regulatory protocols.

Thus, ethical and regulatory aspects form an inseparable dimension of clinical practice involving ketamine. The anesthesiologist, alongside the psychiatrist, must be aware not only of the technical requirements of administration but also of the moral and legal implications of the therapy. This shared responsibility ensures that therapeutic innovation proceeds in a balanced manner, respecting both science and human dignity.

7. Future Perspectives and Multidisciplinary Integration

Future prospects for the use of ketamine in the treatment of resistant depression point to a growing consolidation of its clinical applicability, associated with the development of more refined protocols and the integration of new health technologies. Expanding research seeks to better understand its mechanisms of action, with a focus on investigating biomarkers capable of predicting response to treatment. This personalized approach could represent a significant advance, allowing therapy to be targeted to specific patient profiles, increasing efficacy and minimizing risks.

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The anesthesiologist's role is likely to expand in this scenario, consolidating their participation in multidisciplinary mental health teams. This professional's training in pharmacology, physiology, and critical care management makes them essential for procedural safety. Furthermore, clinical practice has shown that the anesthesiologist's presence builds confidence in both patients and psychiatrists, promoting greater treatment adherence and establishing a more solid and safe therapeutic relationship.

Another promising field is the combination of ketamine with structured psychotherapeutic interventions. Research suggests that substance-induced neuronal plasticity can enhance the effectiveness of cognitive and behavioral therapies, promoting lasting changes in thought and behavior patterns. This integrative model, in which the pharmacological effect acts as a facilitator of psychotherapeutic intervention, could redefine the way psychiatry approaches refractory cases.

Technological innovations also offer new possibilities. The use of remote monitoring devices, artificial intelligence, and big data can optimize the monitoring of patients undergoing treatment, providing real-time information and enabling individualized adjustments. These tools, when integrated into clinical practice, strengthen multidisciplinary approaches and raise the bar for safety and efficiency in the management of resistant depression.

There are also prospects for the development of new ketamine-derived compounds. Molecules such as esketamine and arketamine are being studied with the aim of reducing adverse effects and extending the duration of antidepressant effects. These pharmacological advances may contribute to the creation of safer and more accessible therapeutic options, paving the way for the widespread incorporation of this treatment into healthcare systems.

Medical training will also need to adapt to this emerging reality. Including content on the use of ketamine in psychiatry in the training of anesthesiologists and psychiatrists will be essential to ensure professionals are prepared and aware of the specificities of this practice. Furthermore, continuing education and multidisciplinary training should be encouraged, reinforcing the culture of interdisciplinarity in medicine.

Thus, future prospects not only consolidate ketamine as a therapeutic resource but also highlight the importance of an integrated, multidisciplinary model. By bringing together psychiatrists, anesthesiologists, and other healthcare professionals around a common goal, medicine is strengthened as a science and humanized practice, capable of offering innovative responses to complex clinical challenges.

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Conclusion

The analysis of the anesthesiologist's multidisciplinary role in administering ketamine for treatment-resistant depression highlights the complexity and relevance of this practice in contemporary medicine. The interface between anesthesiology and psychiatry emerges as an innovative model, in which the anesthesiologist's technical expertise ensures procedural safety and the psychiatrist's clinical perspective guides treatment. This partnership represents a paradigmatic advancement, promoting greater efficacy and safety in therapeutic management.

The impact of ketamine as a rapid and effective antidepressant in refractory cases cannot be underestimated. By providing a response within hours, the substance breaks with the logic of traditional antidepressants, whose effects are often delayed and limited. This characteristic becomes particularly valuable in emergency situations, such as in patients at risk of suicide, where rapid intervention can save lives.

However, the transience of effects and the heterogeneity of responses reinforce the need for well-structured protocols. Ketamine administration should not be seen as an isolated solution, but as part of an integrated therapeutic package, which may include psychotherapy, maintenance pharmacotherapy, and multidisciplinary monitoring. This holistic approach increases the chances of success and reduces the possibility of relapse.

The ethical and regulatory aspects discussed demonstrate that scientific enthusiasm must go hand in hand with prudence. The potential for abuse of ketamine and its long-term implications require a cautious approach from healthcare institutions, ensuring that treatment is carried out responsibly, transparently, and fairly. This requires not only technical standards but also public policies that ensure equitable access to this resource.

Future prospects, integrating new technologies, psychotherapy, and pharmacological advances, point to a promising scenario in which ketamine can be used in an increasingly safe and personalized manner. The role of the anesthesiologist, in this context, is likely to expand, consolidating their position as a central figure in innovative psychiatric practice, reinforcing the interdisciplinary nature of modern medicine.

The social impact is also noteworthy. By reducing disabling symptoms and promoting functional recovery, ketamine contributes not only to individual well-being but also to reducing the social and economic costs associated with resistant depression. This is a collective benefit that extends beyond the clinical sphere, reaching the realm of public health policy.

Another relevant point of the analysis is the humanization of care. Patients with TRD often experience long periods of frustration and hopelessness. The possibility of a rapid response with ketamine, combined with close monitoring by specialized professionals, promotes

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trust, adherence, and a renewed sense of the possibility of improvement. This subjective dimension is as important as clinical parameters, as it strengthens the therapeutic bond.

In summary, the administration of ketamine in treatment-resistant depression opens a new chapter in psychiatry and reaffirms the importance of anesthesiologists as key players in clinical safety. The future of this practice will depend on the continued production of scientific evidence, the consolidation of regulatory protocols, and the maintenance of an ethical and humane perspective. Only then will it be possible to transform a promising innovation into a consolidated practice capable of offering hope to millions of patients around the world.

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